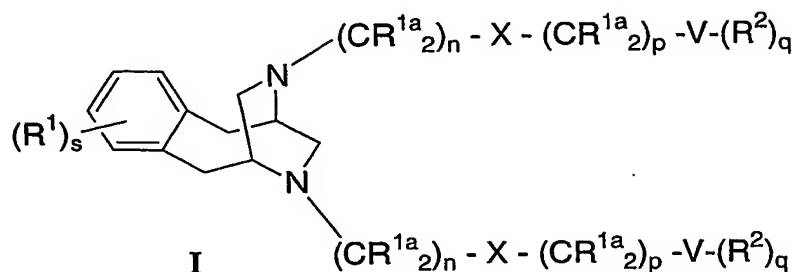


## WHAT IS CLAIMED IS:

1. A compound of Formula I



5 wherein

R<sup>1a</sup> is independently selected from

- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl, and
- 10 3) OR<sup>4</sup>;

R<sup>1b</sup> is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

15

X is independently selected from

- 1) a bond,
- 2) C(O),
- 3) O,
- 20 4) NR<sup>4</sup>,
- 5) S(O)<sub>m</sub>R<sup>4</sup>,
- 6) C(O)OR<sup>4</sup>, and
- 7) C(O)N(R<sup>4</sup>)<sub>2</sub>;

25 R<sup>1</sup> is independently selected from

- 5
- 1) H,
  - 2) halo,
  - 3) OR<sup>4</sup>,
  - 4) NO<sub>2</sub>,
  - 5) -S(O)<sub>m</sub>R<sup>4</sup>,
  - 6) CN
  - 7) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
  - 8) unsubstituted or substituted aryl,
  - 9) unsubstituted or substituted C<sub>2</sub>-C<sub>6</sub> alkenyl,
  - 10) unsubstituted or substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,
  - 11) unsubstituted or substituted C<sub>2</sub>-C<sub>6</sub> alkynyl,
  - 12) unsubstituted or substituted heterocycle,
  - 13) -C(O)R<sup>4</sup>,
  - 14) C(O)OR<sup>4</sup>,
  - 15) C(O)N(R<sup>4</sup>)<sub>2</sub>,
  - 16) S(O)<sub>m</sub>N(R<sup>4</sup>)<sub>2</sub>, and
  - 17) N(R<sup>4</sup>)<sub>2</sub>;

V is independently selected from

- 20
- 1) H,
  - 2) CF<sub>3</sub>,
  - 3) aryl,
  - 4) heterocycle, and
  - 5) C<sub>3</sub>-C<sub>10</sub> cycloalkyl;

25

R<sup>2</sup> is independently selected from

- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,

- 5
- 3)  $-(CR^{1b})_tOR^4$ ,
  - 4) Halo,
  - 5) CN,
  - 6)  $NO_2$ ,
  - 7)  $CF_3$ ,
  - 8)  $-(CR^{1b})_tN(R^4)_2$ ,
  - 9)  $-C(O)OR^4$ ,
  - 10)  $-C(O)R^4$ ,
  - 11)  $-S(O)_2R^4$ ,
  - 10 12)  $-(CR^{1b})_tNR^4(CR^{1b})_tR^5$ ,
  - 13)  $-(CR^{1b})_tS(O)_mNR^4$ ,
  - 14)  $-C(O)OR^4R^5$ ,
  - 15)  $-NR^4C(O)R^4$ ,
  - 16) unsubstituted or substituted aryl, and
  - 15 17) unsubstituted or substituted heterocycle;

$R^4$  is independently selected from

- 20
- 1) H,
  - 2) unsubstituted or substituted  $C_1$ - $C_{10}$  alkyl,
  - 3) unsubstituted or substituted  $C_3$ - $C_{10}$  cycloalkyl,
  - 4) unsubstituted or substituted aryl,
  - 5) unsubstituted or substituted heterocycle, and
  - 6)  $CF_3$ ;

25  $R^5$  is independently selected from

- 1) unsubstituted or substituted aryl, and
- 2) unsubstituted or substituted heterocycle;

m is independently 0, 1 or 2;

n is 0 to 6;

p is 0 to 6;

q is 0 to 6, provided that when V is H or CF<sub>3</sub>, q is 0; and

5 s is 0 to 16;

t is independently 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. The compound according to Claim 1, wherein

10 R<sup>1b</sup>, R<sup>4</sup>, R<sup>5</sup> and variables m, n, p, q and t are as defined in Claim 1 and

R<sup>1a</sup> is independently selected from

1) H, and

2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

15

X is independently selected from

1) a bond,

2) -C(O)R<sup>4</sup>, and

3) C(O);

20

R<sup>1</sup> is independently selected from

1) H,

2) halo,

3) OR<sup>4</sup>,

25

4) N(R<sup>4</sup>)<sub>2</sub>,

5) NO<sub>2</sub>, and

6) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl;

V is independently selected from

30

1) H,

- 2)  $\text{CF}_3$ ,
- 3) aryl, and
- 4) heterocycle;

5  $\text{R}^2$  is independently selected from

- 1) H,
- 2) unsubstituted or substituted  $\text{C}_1\text{-C}_{10}$  alkyl,
- 3)  $-(\text{CR}^{1b})_t\text{OR}^4$ ,
- 4) Halo,
- 10 5) CN,
- 6)  $\text{NO}_2$ ,
- 7)  $\text{CF}_3$ ,
- 8)  $-(\text{CR}^{1b})_t\text{N}(\text{R}^4)_2$ ,
- 9)  $-\text{C}(\text{O})\text{OR}^4$ ,
- 15 10)  $-(\text{CR}^{1b})_t\text{S}(\text{O})_m\text{NR}^4$ ,
- 11)  $-(\text{CR}^{1b})_t\text{NR}^4(\text{CR}^{1b})_t\text{R}^5$ ,
- 12)  $-\text{C}(\text{O})\text{OR}^4\text{R}^5$ , and
- 13)  $-\text{NR}^4\text{C}(\text{O})\text{R}^4$ ;

20 s is 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. The compound according to Claim 2 wherein wherein  $\text{R}^{1b}$ , X,  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^4$ ,  $\text{R}^5$  and variables m, s and t are as defined in Claim 2 and

25

$\text{R}^{1a}$  is independently selected from

- 1) H, and
- 2) unsubstituted or substituted  $\text{C}_1\text{-C}_6$  alkyl;

V is independently selected from

- 1) aryl, and
- 2) heterocycle;

5 n is 0 to 3;

p is 0 to 3;

q is 0 to 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

10

4. A compound that is

3-(3-bromobenzyl)-11-methyl-1,2,3,4,5,6-hexahydro-5,2-(epiminomethano)-3-benzazocine;

3-(3-bromobenzyl)-1,2,3,4,5,6-hexahydro-5,2-(epiminomethano)-3-benzazocine;

3,11-bis(3-bromobenzyl)-1,2,3,4,5,6-hexahydro-5,2-(epiminomethano)-3-benzazocine;

11-acetyl-3-(3-bromobenzyl)-1,2,3,4,5,6-hexahydro-5,2-(epiminomethano)-3-benzazocine;

or a pharmaceutically acceptable salt or stereoisomer thereof.

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5. A pharmaceutical composition which is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

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6. A method of modulating the catalytic activity of protein kinases in a mammal in need thereof comprising contacting the protein kinase with a compound of Claim 1.

7. The method of Claim 6 wherein the protein kinase is an RTK.

8. The method of Claim 7, wherein the RTK is selected from IR, IGF-1R and IRR.

9. A method of treating or preventing a PK-related disorder in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

10. A method of Claim 9, wherein the PK-related disorder is an IGF-1R-related disorder selected from:

- 1) cancer,
- 2) diabetes,
- 3) an autoimmune disorder,
- 4) a hyperproliferation disorder,
- 5) aging,
- 6) acromegaly, and
- 7) Crohn's disease.

11. A method of treating cancer in a mammal in need of such treatment comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

12. A method of treating retinal vascularization comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

13. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a second compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,

- 5
- 3) retinoid receptor modulator,
  - 4) a cytotoxic agent,
  - 5) an antiproliferative agent,
  - 6) a prenyl-protein transferase inhibitor,
  - 7) an HMG-CoA reductase inhibitor,
  - 8) an HIV protease inhibitor,
  - 9) a reverse transcriptase inhibitor, and
  - 10) an angiogenesis inhibitor.

10                    14.     The method of Claim 13, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

15                    15.     A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

16.     The method of Claim 15 wherein radiation therapy is also administered.

20                    17.     A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

25                    18.     A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.

30                    19.     The method of Claim 18 wherein the GPIIb/IIIa antagonist is tirofiban.



20. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.